REMARKS

Double Patenting:

Claims 1, 4-10, 13, and 14 have been provisionally rejected under the judicially created doctrine of double patenting over claims 1, 3, 6-7, and 10-18 of copending Application No. 10/780,484. With this Response, Applicants have filed a terminal disclaimer to overcome the rejection.

Rejection of the claims under 35 USC § 102:

Claims 1, 5, 13, and 14 have been rejected under 35 U.S.C. 102(b) as being anticipated by Wolff et al. (U.S. 2001/0044417 ('417)). Applicants respectfully disagree. '417 teaches polymers containing disulfide bonds and nucleic acids, but '417 does not teach covalent attachment of a polynucleotide to a polymer via a disulfide bond. Paragraph 112 (cited by the Action) describes polynucleotide/polymer complexes in which the *polymer* contains disulfide bonds. Paragraph 117 does not teach covalent attachment of a polynucleotide to a functional group that enhances interaction of the polynucleotide with a transfection reagent. In support of the argument, Applicants have filed a Declaration under 35 C.F.R. 1.132. Applicants request reconsideration of the § 102 rejection.

Claims 1, 4-6, 10, and 13-14 have been rejected under 35 U.S.C. 102(e) as being anticipated by Lewis et al. (U.S. 2003/0143204). The Action points to paragraphs 0042, 0112, 0032, and 0120-0128 in support of the rejection. At paragraph 0042, '204 teaches only morpholinos and 2′-O-methyl polynucleotides, and not any other form of modified polynucleotide. Morpholino backbone and 2′-O-methyl polynucleotides are not functional groups that enhance interaction of the polynucleotide with a transfection reagent. At paragraph 0112 and 0120-0128, '204 teaches that delivery polymers (i.e. transfection reagents) can be attached to functional groups via disulfide bonds, but does not teach that attachment of functional groups to polynucleotides via labile bonds. While '204 does teach at paragraph 0032, that the polycation, the siRNA, the polyanion or the amphipathic compound may be modified by attachment of a functional group, '204 does not provide any means for post-synthetically attaching a functional group to an siRNA. The generic statement, in '204, regarding attachment of a "group that enhances delivery" can not be reasonably interpreted to anticipate any and all forms of attachment of any and all molecules to siRNA. In particular, '204 provides no teaching on: a) post-synthetic modification of an RNA,

b) attachment of a group to siRNA via a labile bond, or c) attachment to RNA of a functional group that enhances interaction of the RNA with a transfection reagent. In support of the argument, Applicants have filed a Declaration under 35 C.F.R. 1.132. Applicants request reconsideration of the § 102 rejection.

Rejection of the claims under 35 USC § 103:

Claims 1, 4-9, 13, and 14 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Hughes et al. (U.S. Patent No. 6,169,078), Manoharan, M. (Biochimica et Biophysica Acta 1489, 1999: 117-130) and Goldsborough (WO 01/94626). The Action states that '078 teaches attachment of lipids to DNA via a disulfide bond. Applicants respectfully disagree. '078 teaches only formation of a cationic lipid in which the hydrophobic tail is connected to the polar or charged head group via a disulfide bond. '078 also teaches using these disulfide bond containing lipids to delivery DNA. However, '078 does not teach that the lipid head group can be a nucleic acid or attachment of a lipid to nucleic acid via a disulfide bond. '078 teaches as follows:

> Column 2 lines 54-56 "the subject invention provides a *new class of lipid molecules* for use in non-viral gene therapy"
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> Column 2 lines 63-54: "The novel compounds of the subject invention provide a *disulfide linker between a polar head group and a lipophilic tail group of the lipid*"
>
> Column 4 lines 58-62: "One specific form of attachment as contemplated by the subject invention involves the use of a cationic liposome as the transport molecule to transport DNA into a cell. In this embodiment the *DNA is carried in the endosome of the liposome*."
>
> Column 5 lines 63-65: "The subject invention also provides new methods for the synthesis of *cationic lipids containing a disulfide bond*. In a specific embodiment the cationic lipid is DOGSDSO."

'078 teaches the use of cationic compounds containing disulfide bonds to deliver DNA (column 2 lines 6-7) but not the covalent attachment of nucleic acid to any molecule via a labile bond. The use of cationic lipids is well known in the gene delivery art. Hydrophobic interaction between the tail groups of the lipids holds the lipids together to form a liposome, in a manner analogous to the formation of a membrane. The cationic head groups then interact via electrostatic interaction with negatively charged nucleic acids. Thus, the composition as a whole requires both hydrophobic and electrostatic interactions for stability. Disruption of the link between the

hydrophobic tail group of the lipid and the charged head group, as taught by '078, breaks the linkage between the hydrophobic and electrostatic interactions of the composition, thus "releasing" the nucleic acid. Thus, in the delivery vehicle taught by '078, DNA interacts with the liposome solely via electrostatic interaction due to the charge inherent in the DNA. '078 teaches a labile bond within the transfection reagent itself, and does not teach any modification of the DNA. Applicants request reconsideration of the §102 rejection.

Claims 1, 4-6, 10, 13, and 14 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Wolff et al. (U.S. 2001/0044417 ('417)), Manoharan, M. (Biochimica et Biophysica Acta 1489, 1999: 117-130) and Tuschl et al. (WO 01/94626). Applicants disagree for the reasons stated above in response to the 102 rejection over '417.

Claims 1, 4-9, 13, and 14 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Fosnaugh et al. (U.S. 2003/0143732), Manoharan, M. (Biochimica et Biophysica Acta 1489, 1999: 117-130) and Goldsborough (WO 01/94626). Applicants respectfully disagree. '732 teaches siRNA-conjugates and complexes for delivery of siRNA to cells. '732 does not teach the pairing a functional group with a transfection reagent such that the functional group enhances interaction of the siRNA with the transfection reagent. Nor does the '732 teach any motivation for doing so. '732 teaches: "The use of chemically modified siRNA is expected to improve various properties of native siRNA molecules through increased resistance to nuclease degradation in vivo and/or improved cellular uptake." (paragraph 0026), "modulates the binding affinity between the sense and antisense strand of the siRNA" (paragraph 0097, 0099), "modulate the polymerase activity of a cellular polymerase capable of generating additional endogenous siRNA molecules" (paragraph 0101), "increase bioavailability" (paragraph 0108) '732 does not list enhanced interaction with a transfection reagent as a motivation for modifying the siRNA. Further, '732 teaches only that delivery methods previously known to those skilled in the art are suitable. Applicants request reconsideration of the §102 rejection.

The Examiner's rejections are now believed to be overcome by this response to the Office Action. In view of Applicants' amendment and arguments, it is submitted that claims 1, 4-10, 13, and 14 should be allowable.

Respectfully submitted,

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I hereby certify that this correspondence is being transmitted to the USPTO on this date: 03/19/2008 .

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